Determinants of Lung Cancer Risk in Cigarette Smokers in New Mexico [1,2]

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ABSTRACT—Although cigarette smoking is the strongest known risk factor for lung cancer, the effects of specific smoking practices have not been completely characterized. The present study examines determinants of lung cancer risk in a population-based, case-control study conducted in New Mexico, 1980–82. The study included 521 cases and 769 controls matched for age, sex, and ethnicity. Either the index subjects or their next-of-kin were interviewed in person to obtain a detailed history of cigarette smoking and information concerning other risk factors. With the use of multiple logistic regression, a model was constructed of the effects of amount smoked, duration of smoking, cigarette type, and smoking cessation on lung cancer risk. Among current smokers, risk increased with each additional cigarette smoked per day ($P<.001$). For duration of smoking, the risk per year smoked in individuals 65 years and older was only one-third that in persons under age 65 years. With regard to cigarette type, a somewhat higher risk was found associated with smoking nonfilter cigarettes, but there was no evidence of decreasing risk as the extent of filter smoking increased. Lifelong filter cigarette smokers and smokers of both filter and nonfilter cigarettes were at lower risk than lifelong smokers of nonfilter cigarettes only. In ex-smokers, the pattern of variation of relative risk with amount and duration was similar to that in the current smokers. Excluding those who had stopped for 1 year or less, the relative risk declined exponentially with duration of smoking cessation ($P<.01$). These analyses confirm the strong benefits of smoking cessation and indicate possible reduction of risk from smoking filter cigarettes.—JNCI 1986; 76:597–604.

Laboratory and epidemiologic evidence has established a causal association between cigarette smoking and lung cancer (*1, 2*). In the United States, the majority of lung cancers in men and women can be readily attributed to tobacco smoking (*2, 3*). In spite of intensive investigation, important issues related to the association between lung cancer and cigarette smoking are still unresolved (*4*). While dose-response relationships with intensity of cigarette consumption have been demonstrated, other determinants of risk for lung cancer in smokers remain largely unknown. Commercial cigarettes have continuously evolved through the addition of filters and other modifications designed to reduce tar and nicotine yields (*4, 5*). Reduced risks would be anticipated for low-yield cigarettes; however, methodologic barriers constrain epidemiologic investigations of low-yield cigarettes and beneficial consequences of smoking them have not been fully established. In fact, since extensive modification of the cigarette began in the 1950's, it has only recently become possible to investigate smokers with predominant use of the newer products.

In New Mexico, the descriptive epidemiology of lung cancer differs in the State's Hispanic and non-Hispanic whites (*6*). We have conducted a population-based, case-control study of incident lung cancer cases, 1980–82, designed to explain the differing occurrence of lung cancer in these 2 ethnic groups. The study questionnaire assessed lifetime smoking habits, occupational history, residence history, dietary intake of vitamin A, and other risk factors. Results related to ethnicity, vitamin A, and occupation have been reported elsewhere (*7–9*). In this paper, we have used the detailed smoking history to examine dose-response relationships and the effects of consuming different types of cigarettes.

METHODS

Case selection.—The present analyses involve subjects in a population-based, case-control study of lung cancer in New Mexico. The cases were ascertained statewide by the New Mexico Tumor Registry, a participant in the Surveillance, Epidemiology, and End Results Program of the National Cancer Institute (*10*). The eligibility criteria limited the series to non-Hispanic and Hispanic white State residents, ages 25 through 84 years, with primary lung cancer other than alveolar cell carcinoma, diagnosed between January 1, 1980, and December 31,

ABBREVIATION USED: OR=odds ratio(s).

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1982. All cases in Hispanics and in non-Hispanic whites below age 50 were included. Non-Hispanic whites, 50 years of age and older, were randomly sampled at a fraction of 0.40 for males and 0.50 for females.

This report is based on the 521 cases interviewed as of August 1, 1983. The diagnosis was established by histology, cytology, or autopsy for 96.4% of the cases and in the remainder by clinical evidence. The overall participation rate either by the cases ($n=274$) or by surrogate respondents ($n=247$) was approximately 91%.

Control selection.—The control series was frequency matched to the cases by age, sex, and ethnicity, at an overall ratio of approximately 1.5 controls per case. Two methods of control selection were employed. First, lists of randomly generated residential telephone numbers were screened to identify potential controls. The screening algorithm required at least 6 calls, which covered weekdays, evenings, and weekends. For each household, the age, sex, and ethnicity of all adults were obtained. Individuals in the appropriate strata of age, sex, and ethnicity were then selected for interview, but only one was taken from each household. Of the 2,108 households contacted, a household census was refused by 287 (14.2%). Second, because this method did not efficiently identify controls over age 65 years, we also sampled from a randomly generated list of New Mexico Medicare participants. According to the Health Care Financing Administration, over 97% of the State's population, 65 years of age and older, is included on the organization's roster. The overall participation rate by persons identified through these two approaches was 83%.

Data collection.—Interviews were conducted by bilingual interviewers according to a standardized protocol. With the exception of 35 respondents contacted by telephone and 4 cases interviewed in the hospital, all interviews were conducted in person in the homes of the cases and controls. The questionnaire obtained information concerning residence history, occupational history, family and personal history of respiratory diseases, and diet. A detailed history of cigarette use was collected for individuals who had smoked for 6 months or more. Because cigarette smokers often stop and then resume smoking, a history was obtained for each time period of cigarette use including the years of starting and stopping, the average number of cigarettes smoked per day, and the number of years that hand-rolled, commercial filter, and commercial nonfilter cigarettes were each smoked. A single question was asked about depth of inhalation, which was characterized as: into the mouth only, into the back of the throat, into the top of the lungs, or deep into the lungs.

Data analysis.—For the present analyses, cigarette smokers were defined as individuals who had smoked cigarettes for at least 6 months. Current smokers were using cigarettes at the time of interview or had stopped smoking within 1 year of the interview. Ex-smokers had stopped smoking permanently more than 1 year before the interview.

The smoking history information was used to calculate various indices of exposure to cigarette smoke (table 1). The total duration (V_9-V_{12}, V_{13}) of cigarette smoking was calculated as the sum of the individual periods of use. The average number of cigarettes smoked per day (V_4-V_7, V_8) was the time-weighted average of the number of cigarettes smoked in each period. With regard to the types of cigarettes that were smoked, two sets of variables were created. First, the percentage of the smoking duration that involved filter cigarettes was calculated and used to create 5 indicator variables (V_{16}-V_{20}) and a continuous variable (V_{21}). The second set of variables was the actual number of years that filter and nonfilter cigarettes were smoked (V_{14}, V_{15}). For these analyses, the nonfilter category included hand-rolled and commercial nonfilter cigarettes.

Conventional stratified analysis and multiple logistic modeling were employed. As required by the frequency matching in the study's design, all analyses included appropriate adjustment for age, sex, and ethnicity. For current smokers, we first used the Mantel-Haenszel method to calculate relative risk estimates separately for the effects of amount and duration with adjustment for age (2 strata), sex, and ethnicity (*11, 12*). In this paper, we provide the Mantel-Haenszel age-specific OR and the Mantel extension χ, which tests for linear trend in risk with increasing dose (*12, 13*). For empty cells, 0.5 was added as appropriate (*12, 13*).

To examine further the effects of the various measures of cigarette smoking, we used multiple logistic regression models that were initially developed separately for the current smokers and ex-smokers of cigarettes (*14, 15*). We evaluated effect modification, i.e., whether the level of the one variable modifies the effect of another,

TABLE 1.—*Measures of tobacco smoking used in the analyses*

Variable	Measures
V_1	Current smoker (1 = current; 0 = never)
V_2	Ex-smokers (1 = ex; 0 = current)
V_3	Age (1 = <65 yr old; 0 = ≥65 yr old)
V_4	Amount 1 (1 = 1-15 cigarettes/day; 0 = else)
V_5	Amount 2 (1 = 16-20 cigarettes/day; 0 = else)
V_6	Amount 3 (1 = 21-30 cigarettes/day; 0 = else)
V_7	Amount 4 (1 = ≥31 cigarettes/day; 0 = else)
V_8	No. of cigarettes smoked/day (continuous)
V_9	Duration 1 (1 = 1-29 yr; 0 = else)
V_{10}	Duration 2 (1 = 30-39 yr; 0 = else)
V_{11}	Duration 3 (1 = 40-49 yr; 0 = else)
V_{12}	Duration 4 (1 = ≥50 yr; 0 = else)
V_{13}	Years of smoking (continuous)
V_{14}	Years of filter smoking (continuous)
V_{15}	Years of nonfilter smoking (continuous)
V_{16}	Filter (1 = filter only; 0 = else)
V_{17}	High filter (1 = 67-99% filter; 0 = else)
V_{18}	Medium filter (1 = 34-66% filter; 0 = else)
V_{19}	Low filter (1 = 1-33% filter; 0 = else)
V_{20}	Nonfilter (1 = nonfilter only; 0 = else)
V_{21}	Percent of smoking duration involving filter use (continuous)
V_{22}	Inhale (1 = top of lungs or deep into lungs; 0 = mouth or back of throat)
V_{23}	Years of smoking cessation (continuous)
V_{24}	Pipe (1 = if ever-pipe use; 0 = else)
V_{25}	Cigar (1 = if ever-cigar use; 0 = else)

TABLE 2.—*Ethnic, sex, and age distribution of cases and controls by cigarette smoking status in a case-control study of lung cancer in New Mexico, 1980–82*

Ethnic group	Sex	Age, yr	Cigarette smoking status					
			Current smoker		Ex-smoker		Never-smoker	
			No. of cases	No. of controls	No. of cases	No. of controls	No. of cases	No. of controls
Non-Hispanic whites	♂	<65	69	54	18	59	1	35
		≥65	74	58	54	99	6	60
	♀	<65	45	35	8	17	2	47
		≥65	34	14	18	19	11	52
Hispanics	♂	<65	24	22	8	18	0	9
		≥65	38	30	17	28	2	21
	♀	<65	12	8	3	7	2	27
		≥65	15	6	4	5	4	34

by adding product terms to the models or by running the models within specific subsets of the subjects. We assessed possible bias introduced by next-of-kin interviews by performing the analyses separately within groups defined by interview type.

Two sets of models were used for the current smokers, depending on the hypotheses that were being tested; in some, never-smokers were the reference category, whereas in others, only current smokers were included. In models including never-smokers, the value of zero was assigned to the amount and duration variables for never-smokers. Because we found strong and statistically significant interaction between age and duration of smoking, their product was included in all models. To evaluate the effect of types of cigarettes smoked, we used two distinct approaches. In the first approach, we added either the continuous or categorical measures of filter cigarette use to the model that included amount and duration. In the second approach, the duration of smoking was replaced by 2 variables: the years of filter use and the years of nonfilter use, which together summed to the total duration. For never-smokers, these variables assumed the value of zero.

Similar models were developed for the ex-smokers, but all models included the duration of smoking cessation. Standard programs of the Statistical Analysis System (SAS) were used for all analyses (*16*).

RESULTS

The analyses were limited to the 469 cases and the 764 controls with complete information on current cigarette smoking status, amount smoked, and duration of cigarette smoking (table 2). Comparison of the excluded 52 cases and 5 controls with the included subjects showed no differences in the ethnic and sex distributions, but the excluded subjects were significantly older and a higher proportion of surrogate interviews had been necessary for them.

Initially, using stratified analysis, we examined the effects of duration and amount of smoking in current smokers. With never-smokers as the reference category, the age-, sex-, and ethnicity-adjusted OR for lung cancer increased significantly with increasing duration (Mantel extension $\chi=13.9$; $P<.001$) and amount smoked daily (Mantel extension $\chi=14.7$; $P<.001$). The slope of the dose-response relationships for effects of amount and the duration of smoking decreased with increasing age. Because the effects of duration were similar for the age categories below age 65 years (<55, 55–64) and those 65 years or older (*65–74, 75–84*), we stratified at age 65 years for the present analyses (table 3). With the never-smokers as the reference category, significant linear trends in OR with increasing duration of smoking were observed for both age groups. However, the OR for smokers of 30 years' duration or more were strongly affected by age, with much lower values for those 65 years of age and older.

We further restricted the analysis to current smokers to eliminate the effect of rising lung cancer risk with age in the never-smokers (table 4). For those less than 65 years of age, the OR rose with increasing duration (Mantel extension $\chi=4.1$; $P<.001$ and amount of smoking (Mantel extension $\chi=4.8$; $P<.001$). In contrast, for those 65 years of age and above, no significant increase in risk with increasing duration of smoking was observed (Mantel extension $\chi=0.50$; not significant), but the effect of amount of smoking remained statistically significant (Mantel extension $\chi=3.5$; $P<.001$).

For the simultaneous examination of amount and duration of smoking, the indicator variables corresponding to the categories in the stratified analysis were entered into multiple logistic regression models. Separate analyses were performed for the 2 age groups less than 65 years and 65 years or older. For smokers less than 65 years of age, linear dose-response relationships of log odds were observed for amount and duration of smoking. For smokers 65 years or older, the log odds increased significantly with amount but not with duration of smoking.

Because linear trends in log odds were observed in these analyses, in subsequent models the dose measures for amount and duration were the continuous variables V_8 and V_{13}, respectively. The logistic regression coefficients for the amount and duration of smoking effects are presented in table 5 for the different populations of

TABLE 3.—*Adjusted[a] OR for lung cancer by age, duration of smoking, and number of cigarettes smoked daily in current smokers relative to never-smokers in a case-control study of lung cancer in New Mexico, 1980–82*

Variable	<65 yr old			≥65 yr old		
	No. of cases	No. of controls	OR	No. of cases	No. of controls	OR
Duration of cigarette smoking						
Never smoked	5	118	1.0[b]	23	167	1.0[b]
1–29 yr	13	31	12.9	7	2	22.9
30–39 yr	61	50	37.3	7	8	6.6
40–49 yr	68	36	57.3	36	23	11.7
50–59 yr	8	2	91.4	82	53	16.1
≥60 yr	—	—	—	29	22	11.9
No. of cigarettes daily						
Never smoked	5	118	1.0[b]	23	167	1.0[b]
1–15	17	33	16.2	40	44	8.6
16–20	44	45	27.6	64	43	12.3
21–30	33	22	47.1	22	10	22.9
≥31	56	19	89.3	35	11	24.3

[a] Adjusted for sex and ethnicity.
[b] $P<.001$ for the Mantel extension χ for linear trend.

TABLE 4.—*Adjusted[a] OR for lung cancer by age and duration of smoking in current smokers only in a case-control study of lung cancer in New Mexico, 1980–82*

Duration of cigarette smoking, yr	OR[b] for individuals <65 yr old	OR[b] for individuals ≥65 yr old	OR[c] for individuals ≥65 yr old
1–29	1.0[d]	1.0[e]	1.0[f]
30–39	3.0	0.3	
40–49	4.8	0.6	1.1
50–59	7.9	1.8	1.7
≥60	—	0.4	1.1

[a] Adjusted for sex and ethnicity.
[b] Smokers of 1–29 years' duration as the reference category.
[c] Smokers of 1–39 years' duration as the reference category.
[d] Mantel extension χ for trend = 4.0; $P<.001$.
[e] Mantel extension χ for trend = 0.4; not significant.
[f] Mantel extension χ for trend = 0.3; not significant.

TABLE 5.—*Logistic regression coefficients for estimation of lung cancer risk associated with amount smoked and duration of smoking in current smokers and ex-smokers in a case-control study for lung cancer in New Mexico, 1980–82*

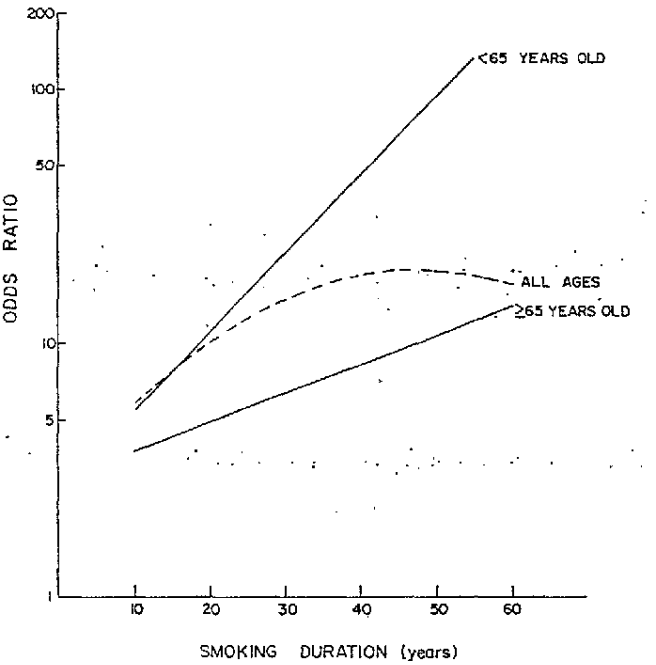
Models[a]	Logistic regression coefficients for various cigarette smoking groups								
	Current smoker and never-smoker[b]			Current smoker only			Ex-smoker only		
	<65 yr old	≥65 yr old	All ages	<65 yr old	≥65 yr old	All ages	<65 yr old	≥65 yr old	All ages
Amount (V_3), cigarettes/day	0.050[c]	0.054[c]	0.052[c]	0.052[c]	0.053[c]	0.052[c]	0.049[c]	0.016	0.023[c]
Duration (V_{13}), yr	0.071[c]	0.024[c]	0.026[c]	0.087[c]	−0.010	−0.010	0.069[d]	−0.010	−0.008
Age-duration interaction ($V_3 \times V_{13}$)			0.046[c]			0.098[c]			0.069[d]
Years of smoking cessation (V_{23})							−0.068	−0.078[d]	−0.073[c]

[a] All models included appropriate adjustment for age, sex, and ethnicity.
[b] Never-smokers are included with the natural values of 0 yr and 0 cigarettes/day.
[c] $P<.001$.
[d] $P<.05$.

smokers. The logistic coefficient for (V_8) estimates the increase in log odds for each additional cigarette smoked per day. Using the interaction term ($V_3 \times V_8$), we found no effect modification by age for amount. The coefficient for duration (V_{13}) provides the estimate of change in log odds from 1 year of smoking for individuals 65 years of age or older. The coefficient for interaction between age and duration ($V_3 \times V_{13}$) estimates the excess in log odds from 1 year of smoking in those younger than age 65, relative to the older smokers. This interaction term was significant for both current smokers and ex-smokers. Using the logistic coefficients from the model including never-smokers and current smokers, we calculated the OR for a current smoker of given duration, relative to a never-smoker (text-fig. 1). When the interaction variable between age and duration is not included in the model, a significant quadratic effect of duration is observed ($b = -8.6 \times 10^{-4}$; $P < .005$) (text-fig. 1).

The effects of amount and duration of smoking, with adjustment for cessation, were the same for ex-smokers and current smokers (table 5). The lower logistic coefficient for amount smoked in ex-smokers 65 years and older did not differ significantly from the logistic coefficients in the current smokers and younger ex-smokers. We used a combined model for current smokers and ex-smokers to estimate the decline in risk with smoking cessation. The risks in the ex-smokers were compared to those in a current smoker who continued to smoke the same amount while accumulating additional years of smoking duration, in comparison to the smoking duration in ex-smokers. The OR for ex-smokers below age 65 years declined to 0.49, 0.24, and 0.06 for 5, 10, and 20 years of smoking cessation, respectively; for those older than 65 years, the corresponding OR were 0.73, 0.54, and 0.29.

Two approaches were used to evaluate the effect of cigarette type on lung cancer risk in the current smokers. First, we employed indicator variables (V_{16}-V_{20}) or a continuous variable (V_{21}) that represented the proportion of the years of smoking that involved filter cigarettes. Second, we partitioned the duration (V_{13}) into



TEXT-FIGURE 1.—OR for lung cancer, by age group, in current smokers of 20 cigarettes per day, relative to never-smokers (OR for never-smokers = 1).

years of filter (V_{14}) and years of nonfilter (V_{15}) use. Because the smoking practices of the Hispanic and non-Hispanic whites differed, we performed the analyses separately for the 2 ethnic groups. At all ages, a higher proportion of Hispanic males and females had ever smoked hand-rolled cigarettes in comparison with the non-Hispanic whites. The differences were more prominent among cases. The average duration of smoking hand-rolled cigarettes was also longer in the Hispanics (table 6). Initial separation of the nonfilter cigarettes into commercial and hand-rolled types showed that generally higher risks were associated with smoking hand-rolled as compared to commercial nonfilter ciga-

TABLE 6.—*Average years of smoking specific types for current smokers who ever used a given type by age, sex, ethnicity, and case-control status in a case-control study of lung cancer in New Mexico, 1980–82*

Sex	Age, yr	Status	Average yr of smoking					
			Hand-rolled cigarettes		Commercial nonfilter cigarettes		Filter cigarettes	
			Non-Hispanic whites	Hispanics	Non-Hispanic whites	Hispanics	Non-Hispanic whites	Hispanics
Male	<65	Case	7.0	18.4	22.5	22.5	20.8	22.7
		Control	7.9	7.1	18.9	13.9	18.1	20.0
	≥65	Case	12.5	24.1	32.8	30.1	19.4	14.2
		Control	9.9	16.0	27.9	27.3	24.5	20.0
Female	<65	Case	4.3	18.3	18.8	21.0	20.5	15.2
		Control	6.0	2.0	15.1	17.2	21.6	15.3
	≥65	Case	9.5	31.7	29.8	30.6	21.4	16.4
		Control	3.0	35.0	29.6	14.3	17.9	25.8

rettes, but the differences were not significant in any of the age-sex-ethnic strata. Consequently, commercial nonfilter and hand-rolled cigarettes were combined into one nonfilter category.

The effects of filter cigarette smoking differed in the Hispanic and the non-Hispanic whites (table 7). In the Hispanics, the OR declined consistently as the proportion of filter cigarette smoking increased; in the non-Hispanic whites, filter use was associated with lower OR, but a dose-response relationship with the percentage of filter use was not evident. When V_{21} was substituted for V_{16}–V_{20}, there was significant reduction in risk for lung cancer with increased filter use in the Hispanics ($b = -0.024$ per percent; $P<.001$), but not in the non-Hispanic whites ($b = -0.004$ per percent; $P=.30$).

Partitioning the duration into years of filter use and years of nonfilter use showed a similar pattern by ethnic group (table 8). In the non-Hispanic whites, the coefficients for the 2 separate cigarette-type variables were similar. In the Hispanics, nonfilter smoking was associated with a significantly higher risk ($P<.05$). Our conclusions did not change when all individuals who ever smoked hand-rolled cigarettes were eliminated from the analysis.

Because 47% of the case interviews had been with next-of-kin, all the logistic analyses were performed separately within the self-reported and next-of-kin groups. The results for the 2 interview groups were comparable and did not alter our interpretation of the analyses.

The effect of depth of inhalation was evaluated only for current smokers with self-reported data. Smokers who reported inhalation into the top of the lungs or deep into the lungs were at increased risk (OR=2.1; $P<.005$) compared with those who reported inhaling into the mouth or the back of the throat only. We tested for modification of the effect of inhalation by amount smoked; within strata of amount smoked, less than 20 or 20 or more cigarettes daily, the logistic regression coefficients for the indicator variable for inhalation were $b=0.54$ ($P=.18$) and $b=0.80$ ($P<.05$) for the lighter and heavier smoking groups, respectively. When the groups were combined, an interaction term for a differing effect of inhalation with amount smoked was not statistically significant ($P=.40$).

We evaluated the effect of ever-pipe and ever-cigar use by adding variables V_{24} and V_{25} to the models. The logistic regression coefficients for these 2 variables were insignificant, and their values did not indicate important effects on risk.

TABLE 7.—*Ethnic-specific OR for lung cancer in current smokers by the proportion of years that filter cigarettes were used in a case-control study of lung cancer in New Mexico, 1980–82*

Models[a]	OR in:	
	Non-Hispanic whites	Hispanics
Filter only (V_{16})	0.80	0.04[b]
67–99% filter (V_{17})	0.71	0.26[b]
34–66% filter (V_{18})	0.58	0.39
1–33% filter (V_{19})	0.83	0.56
Nonfilter only (V_{20})[c]	1.00	1.00

[a] In addition to age, sex, and ethnic variables, V_8 (amount), V_{13} (duration), and $V_8 \times V_{13}$ (age-duration interaction) were included in the models.
[b] $P<.05$.
[c] Reference category.

TABLE 8.—*Age- and ethnic-specific logistic coefficients for estimation of lung cancer risk associated with duration of filter and nonfilter cigarette use in a case-control study of lung cancer in New Mexico, 1980–82*

Models[a]	Logistic coefficients in:			
	Non-Hispanic whites		Hispanics	
	<65 yr old	≥65 yr old	<65 yr old	≥65 yr old
Amount (V_8)	0.049[b]	0.055[b]	0.053[c]	0.066[c]
Filter duration (V_{14})	0.065[b]	0.010	0.052	0.002
Nonfilter duration (V_{15})	0.064[b]	0.026[c]	0.110[b]	0.037[c]

[a] Adjusted for age and sex.
[b] $P<.005$.
[c] $P<.05$.

DISCUSSION

This study involved incident lung cancer cases from 1980 through 1982 in New Mexico's Hispanic and non-Hispanic whites. We confirmed findings from other populations with regard to dose-response relationships between lung cancer risk and measures of smoking and the reduction of risk that follows smoking cessation. The collection of detailed smoking information approximately 30 years after the widespread introduction of filter cigarettes facilitated an examination of the risks of smoking different types of cigarettes.

We assessed the effects of cigarette type with two distinct modeling approaches and did not find strong benefits from smoking filter cigarettes (tables 7, 8). Cigarette type had differing consequences in the Hispanic and non-Hispanic whites (table 8). On average, the former group had smoked hand-rolled cigarettes for more years (table 6) than the latter group and the smoking habits of the 2 groups may differ in other respects as well (*8*). The findings from the non-Hispanic whites can be more readily generalized to other cigarette smokers in the United States.

In the non-Hispanic whites, we found somewhat higher risks associated with smoking nonfilter cigarettes, but we found no evidence of increasing protection with the extent of filter smoking. While few lifelong filter smokers were included, the OR estimate associated with this pattern was comparable to that for smokers of mixed types. Lubin et al. (*17, 18*) recently reported similar analyses from an extremely large case-control study in Western Europe. The relative risk for lifelong nonfilter cigarette smokers was approximately twice that for

smokers of filter cigarettes alone. However, dose-response relationships could not be demonstrated between relative risk and the proportion of years nonfilter brands were smoked or with a cigarette tar index. Among sustained smokers, switching from nonfilter to filter cigarettes was associated with a small reduction in risk (*17*). The results from another recent case-control study conducted in Cuba also did not show a convincing association between tar intake and relative risk of lung cancer (*19*). In a prospective study of British male civil servants, tar yield was associated with lung cancer in noninhalers but not in inhalers (*20*). In the United States, investigations spanning the 1960's and 1970's have shown reduced risks in smokers who switched from nonfilter to filter cigarettes (*21–24*). Thus our results are supported by other studies that show the highest relative risks in sustained nonfilter cigarette smokers and no clear evidence of declining risks with increasing use of filter cigarettes. We interpret the apparently discrepant findings in Hispanics as reflecting the higher risks associated with the smoking of nonfilter cigarettes by this group (table 8); as the proportion of filter cigarette smoking decreases, that of nonfilter cigarette smoking rises and risk increases.

In the non-Hispanic whites, the lack of a dose-response relationship with extent of filter smoking may be explained by methodologic and biologic considerations. We could not estimate total tar intake satisfactorily with our questionnaire. Thus the indices of cigarette type that we used may misclassify the subjects' carcinogens. Inaccurate recall of the details of smoking cigarette types may also introduce misclassification. Alterations of smoking pattern following the switch from nonfilter to filter cigarettes may partially compensate for the reduced tar and nicotine yields of the filter products, as assessed by a machine (*5*).

We readily confirmed the reduction in risk that follows cessation of cigarette smoking. The case series included 130 ex-smokers; some had stopped smoking as long as 54 years previously. As in other series (*17*), the risk of lung cancer in ex-smokers, in comparison with that in continuing smokers, declined steadily with the duration of cessation.

Persons reporting that they inhaled cigarette smoke more deeply were at increased risk. The results of other studies on the consequences of reported inhalation practices are conflicting. In the cohort of British doctors, noninhalers had higher lung cancer mortality (*25*). Higenbottam et al. (*20*) reported similar findings from two separate cohort studies: the Whitehall study of British civil servants and the U.S.–U.K.–Norwegian migrants study. In these studies, smokers of 20 or more cigarettes daily, who reported deeper inhalation, had lower lung cancer mortality. Wald et al. (*26*) have suggested that the increased risks in noninhalers reflect increased tar deposition in the proximal airways of the upper lobes. However, other studies, in addition to the present one, have demonstrated higher risks in inhalers than in noninhalers (*18, 19, 27*). Unfortunately, none of the inhalation questions used in these studies have been validated against appropriate physiologic measures. In a study of 10 subjects, Tobin and Sackner (*28*) found that reported inhalation practices were not consistent with actual inhalation pattern, as measured with a nonobtrusive device.

An unexpected finding was the strong interaction between age and duration of cigarette smoking. Both stratified (tables 3, 4) and logistic approaches (table 5) demonstrated a statistically significant reduction in the effect of smoking duration as age increased, but a similar interaction was not present between age and the number of cigarettes smoked. Detection of statistically significant interaction is model dependent (*29*). Since these data were analyzed with logistic regression, the finding of interaction between age and duration implies departure from the multiplicative scale.

In populations with a high incidence of lung cancer, cross-sectional, age-specific incidence and mortality rates generally decline in the older age groups. This decline has generally been considered to reflect cohort-specific smoking patterns, though explanations related to underdiagnosis and selective survival of less susceptible individuals have been offered (*2, 30, 31*). In their analysis of lung cancer incidence in the cohort of British doctors, Doll and Peto (*31*) also detected apparently reduced risk among older smokers. While lung cancer incidence rose uniformly among regular smokers through age 79 years, the incidence rates declined in older men, even when the rates were standardized for the amount smoked.

Although this decline in effect of smoking duration with age may be interpreted biologically, potential sources of bias should also be considered. In discussing this phenomenon in the cohort of British doctors, Doll and Peto (*31*) considered potential underdiagnosis of lung cancer among the elderly. This explanation is not readily applicable to a case-control study, though disease misclassification, differential on smoking status, might increase with age. With increasing age, the intensity of diagnostic evaluation may lessen and clinical diagnoses without histologic confirmation may be more common in the elderly. Accordingly, lung cancer might be diagnosed more often on clinical evidence in smokers but overlooked in nonsmokers. If such bias does occur, the effect would be an increase with age in measures of association between lung cancer and smoking. Alternatively, misclassification of cigarette smoking variables might be more frequent in the older cases because of less accurate recall by older respondents and an increased proportion of surrogate interviews in the older cases. On the basis of preliminary findings from survey data, Harris (*32*) suggested that accuracy of recall of age of starting and stopping smoking declines with increasing respondent age. In the present study, surrogate interviews were needed more often in older subjects, but the findings were unchanged when the analyses were restricted to the subjects who were directly questioned. Finally, the interaction could reflect unmeasured aspects of cigarette smoking that both influenced the respiratory tract dose of carcinogens and were associated with age.

Alternatively, those who develop lung cancer at

younger ages may be more susceptible to cigarette smoke because of endogenous characteristics or unmeasured environmental factors. The susceptibility explanation implies that the sequence of changes resulting in the development of lung cancer may be influenced by host characteristics and is not solely stochastic.

This study readily confirmed the strong relationship between cigarette smoking and lung cancer. The risk of lung cancer was primarily determined by the amount and duration of cigarette use, but it was modified by types of cigarettes smoked, inhalation practices, and age. However, the findings suggest that the risk of lung cancer in smokers can best be reduced by cessation of smoking.

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